

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau(43) International Publication Date
18 March 2004 (18.03.2004)

PCT

(10) International Publication Number
WO 2004/022758 A1(51) International Patent Classification⁷: C12N 15/66, 15/10, C12Q 1/68(21) International Application Number:
PCT/GB2003/003866(22) International Filing Date:
5 September 2003 (05.09.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0220649.8 5 September 2002 (05.09.2002) GB
0220773.6 6 September 2002 (06.09.2002) GB(71) Applicant (for all designated States except US): PLANT
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WC2B 6HP (GB).(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: GENOME PARTITIONING

(57) **Abstract:** This invention relates to 'genome partitioning' and nucleic library construction, for example for sequence variation discovery and screening. The method employs a plurality of restriction enzymes in order to reliably reproduce a representative partition of the entirety of a sample nucleic acid based on the restriction ends of one or more 'layers' of the fragments present. In preferred embodiments there is provided a method for producing a nucleic acid library, which library contains a plurality of different nucleic acid fragments, the method comprising: (i) digesting the sample nucleic acid with a plurality of different restriction enzymes to generate a plurality of different layers of fragments, wherein each layer is a group of fragments having a unique combination of restriction ends, and wherein the combination of layers represents the entirety of the sample nucleic acid, (ii) optionally purifying said fragments, (iii) selecting a desired sub-set of layers according to the unique restriction ends of said layers, (iv) ligating said sub-set of layers into vectors adapted to receive it, (v) transforming host cells with the vectors (vi) culturing said host cells to provide said library containing said partition of the sample nucleic acid. The invention also provides systems, methods and functions for designing and optimising such libraries, and genotyping 'chips' based on the genome partitioning methods.

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